



# Investigation of prolidase, adenosine deaminase, glutathione s-transferase and glutathione reductase activities in patients with abortus imminens

Abortus imminens hastalarında prolidaz, adenozin deaminaz, glutatyon-s-transferaz ve glutatyon redüktaz aktivitelerinin araştırılması

Some enzyme activities in abortus imminens

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## Öz

**Amaç:** Abortus Imminens gebelikle ilişkili bir hastalıktır ve patofizyolojisi tam olarak belirlenmemiştir. Bu çalışmanın amacı Abortus Imminens hastalarında prolidaz (PR) enzim aktivitesi ile adenozin deaminaz (ADA), glutatyon -S-transferaz (GST) ve glutatyon redüktaz (GR) aktiviteleri arasındaki muhtemel ilişkileri araştırmaktır. **Gereç ve Yöntem:** Abortus Imminensli 50 hasta Haziran 2015 ile Eylül 2015 yılları arasında İpekyolu Kadın ve Çocuk Hastanesi'nde incelendi. Seçilen hastaların yaş aralığı 18-50 arasında idi. Prolidaz (PR) enzim aktivitesi ve adenozin deaminaz (ADA), glutatyon -S-transferaz (GST) ve glutatyon redüktaz (GR) aktiviteleri, Abortus Imminens serumlarında ölçülmüştür. Prolidaz (PR), adenosin deaminaz (ADA), glutatyon-S-transferaz (GST) ve glutatyon redüktaz (GR) aktiviteleri spektrofotometrik olarak belirlendi. **Bulgular:** Abortus Imminens hastalarında sağlıklı bireylere göre glutatyon-S-transferaz ve glutatyon redüktaz aktivitelerinin anlamlı olarak azaldığı bulunmuştur. **Tartışma:** Abortus Imminens'in patogenezinde antioksidan enzim aktivitelerindeki değişiklikler önemli rol oynayabilir. Serum ADA düzeyleri Abortus Imminens'de biyokimyasal bir belirteç olarak kullanılabilir. Bu çalışma Abortus Imminens ve antioksidanlar arasındaki ilişkiyi inceleyen literatürdeki ilk geniş çaplı çalışmadır.

## Anahtar Kelimeler

Abortus Imminens; Antioksidan; Enzim

## Abstract

**Aim:** Abortus Imminens is a pregnancy-related disease, the pathophysiology of which has not yet been thoroughly determined. The aim of this study was to investigate possible relations between prolidase (PR) enzyme activity and adenosine deaminase (ADA), glutathione S-transferase (GST) and glutathione reductase (GR) activities in Abortus Imminens patients. **Material and Method:** Fifty patients with Abortus Imminens were examined in İpekyolu Women's and Children's Hospital between June 2015 and September 2015. The age range of the patients selected was between 18 and 50. Prolidase (PR) enzyme activity and adenosine deaminase (ADA), glutathione S-transferase (GST) and glutathione reductase (GR) activities were measured in Abortus Imminens serums. Prolidase (PR), adenosine deaminase (ADA), glutathione-S-transferase (GST) and glutathione reductase (GR) activities were determined by spectrophotometry. **Results:** Glutathione S-transferase and glutathione reductase activities were found to be significantly decreased in Abortus Imminens patients compared to healthy subjects. **Discussion:** Changes in antioxidant enzyme activities may play a very important role in the pathogenesis of Abortus Imminens. The serum ADA levels can be used as a biochemical marker in Abortus Imminens. This is the first large-scale study in the literature of the relationship between Abortus Imminens and antioxidants.

## Keywords

Abortus Imminens; Antioxidant; Enzyme

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## Introduction

Abortus imminens is vaginal bleeding, despite the presence of a fetus in the uterus, during the first half of pregnancy. In such cases, there is an imminent risk of miscarriage.

As oxidative stress increases, molecules known as hydroxy or peroxy antioxidants minimize the conditions that may lead to an accumulation of free radicals.

Antioxidants such as superoxide dismutase, catalase, glutathione reductase and glutathione-S-transferase are very important molecules which decrease free radicals [1]. GR (EC 1.8.1.7) is an enzyme encoded by the GSR gene in humans [2]. According to the literature, glutathione reductase deficiency has been determined to cause a number of diseases [3]. GST is an important enzyme found in cytosolic, mitochondrial, and microsomal cells [4].

ADA (E.C. 3.5.4.4.) exists in various molecular forms with different molecular weights. It plays an important role as a key enzyme involved in the salvage of purine nucleosides and the recycling of purines [5,6]. However, so far there are no reports available on ADA levels in Abortus Imminens. PR plays an important role in the recycling of proline from imidodipeptides for the resynthesis of collagen and other proline-containing proteins [7]. PR enzyme activity has been found in erythrocytes, leukocytes, plasma, dermal fibroblasts, kidneys, the brain, heart, thymus, and uterus [8].

We aimed to determine the relationship between proliadase (PR) and adenosine deaminase (ADA), glutathione-S-transferase (GST) and glutathione reductase (GR) activities in patients with Abortus Imminens.

## Material and Methods

Fifty patients with Abortus Imminens were examined in Ipekyolu Women's and Children's Hospital in Van, Turkey, between June 2015 and September 2015. In addition, 50 healthy women in the first trimester of pregnancy were selected from Ipekyolu Women's and Children's Hospital for the control group. The age of the patients varied between 18 and 50. Informed consent was obtained from all participants before initiation of the study, which was carried out according to the Helsinki Declaration. We also received approval from the local ethics committee. The serum samples were separated by centrifugation, and the samples were processed immediately. The serum samples were placed in deionized polyethylene tubes and kept at -80°C in a deep-freeze (without thawing) until the day of analysis.

**Biochemical Analysis:**

The ADA activity was measured according to the method used by Giusti. The absorbance was measured at 620 nm with a spectrophotometer [9].

The GR activity was determined spectrophotometrically by using the substrate. The serum samples were measured spectrophotometrically at 340 nm following Beutler method [10].

The PR activity was determined by measurement of proline employing the method proposed by Myara et al., which is a modification of Chinard's method [11,12,13].

The GST activity was measured following Habig et al. [14].

**Statistical analysis:**

All the results are expressed as means and standard deviation (mean  $\pm$  SD). Non-parametric continuous variables were com-

pared by the Mann-Whitney U test. Parametric variables were compared using the Student's t-test. P-values of less than 0.05 were considered statistically significant. Statistical evaluation was carried out using SPSS11.0.

## Results

The GST activity was significantly lower in serum levels of Abortus Imminens patients as a whole compared to the control group ( $P < 0.05$ ) (Table 1). The serum ADA activity was found to be significantly decreased when compared to the control group ( $P < 0.05$ ) (Table 1). The PR enzyme activity was found to be significantly increased when compared to healthy subjects ( $P < 0.05$ ) (Table 1). The GR serum activity was significantly lower in Abortus Imminens compared to the controls ( $P < 0.05$ ) (Table 1).

Table 1 (Results)

	Group	Mean $\pm$ Std. Deviation	Minimum	Maximum	p
ADA (U/L)	Patient	76.88 $\pm$ 18.12	44.32	135.23	0.001
	Control	37.51 $\pm$ 3,43	32.27	42.27	
GR (U/mL)	Patient	0.03 $\pm$ 0.02	0.01	0.06	0.001
	Control	0.59 $\pm$ 0.32	0.17	0.94	
GST(U/L)	Patient	0.03 $\pm$ 0.03	0.01	0.08	0.001
	Control	0.39 $\pm$ 0.42	0.08	0.94	
Prolidase (U/L)	Patient	34.12 $\pm$ 4.29	28.37	42.56	0.001
	Control	0.94 $\pm$ 2.00	59.56	65.48	

## Discussion

Abortus Imminens is vaginal bleeding with mild uterine cramps during the first half of pregnancy and carries the risk of miscarriage. Half of the cases of Abortus Imminens can result in miscarriage [15].

The cell membrane is an important barrier for free radicals [16,17,18]. Free radicals can have significant effects on the immune system, digestive system, heart, lungs, muscle-related diseases, and on many pathological conditions such as aging, atherosclerosis, cancer, diabetes, and rheumatoid arthritis [19]. In biochemical systems catalase (CAT), peroxidase (POD), glutathione reductase (GSSG-Rx) and superoxide dismutase (SOD) are important antioxidant enzymes.

Antioxidants function by preventing free radical formation. According to the literature, studies have shown that antioxidants reduce the effects of free radicals and prevent cell damage.

Abnormal placentation in the first trimester of pregnancy leads to oxidative stress, and endothelial dysfunction caused by oxidative stress plays a key role in the emergence of complications such as miscarriage [20,21].

GR helps to protect human cells from free radicals [22]. The oxidant and antioxidant glutathione, glutathione reductase, catalase, superoxide dismutase, nitric oxide (NO) and malondialdehyde (MDA) levels have been investigated in cases of recurrent pregnancy loss. Antioxidant enzymes such as GR and the total antioxidant capacity have been found to be reduced [21,23]. In a number of studies, the antioxidant GSH and GR activities have been found to be decreased in some diseases of the stomach, liver, and colon [24,25]. Serum GSH, SOD and GPx activities have been found in low levels in primary and metastatic liver cancer. We found low serum GR activity compared with the healthy control group.

In a study conducted on patients with bronchial asthma, there was no significant difference in GR activity [26].

The most important function of GST is detoxification of electrophilic carbon, sulfur, or non-polar substrates of xenobiotics by catalyzing the GSH nucleophilic attack [27]. GST plays an important role in the protective system and the antioxidant defense system in the fight against many diseases in humans [28]. In one study, antioxidant activities were found to be lower in HCC patients when compared to controls [29]. Antioxidant enzyme activities have been found to be reduced in cancer patients [30]. We found low serum GST activities in patients with Abortus Imminens when compared to the healthy control group. ADA is an important enzyme in purine biosynthesis [31]. ADA is particularly sensitive to stimulation by growth factors and cytokines during rapid tissue proliferation [32]. Serum ADA levels have been found to be significantly high in head and neck cancer, brain cancer and also stomach cancer [33,34,35]. The role of ADA in many diseases has been investigated. Serum ADA levels have been found to be significantly high in patients with visceral viral leishmaniasis and bacterial pneumonia, cutaneous anthrax, HIV infection, extra-pulmonary tuberculosis, *H. pylori* infection, acute appendicitis, and mononucleosis [36,37,38,39,40]. In the present study, we found higher serum ADA activity in patients with Abortus Imminens than in the healthy control group. Our findings are similar to those reported in the literature. This study suggests that serum ADA activity can be used as a biochemical marker in Abortus Imminens.

PR plays an important role in collagen turnover, matrix remodeling and cell growth [41]. Prolidase activity has been found with increased levels in a number of clinical studies, foremost in the liver and coronary artery disease [12]. PR activity has been investigated in various diseases such as pancreatic cancer, lung adenocarcinoma, breast cancer, endometrial cancer, stomach cancer and ovarian cancer [42]. In one study, high amounts of prolidase activity were found in the placenta of women who experienced early pregnancy loss [43]. In another study, prolidase activity in the placenta has been found to be high in patients with preeclampsia [44]. In this study, high serum PR activity was found to be significantly higher in Abortus Imminens patients than in the healthy control group.

Serum PR enzyme activity has not previously been investigated in patients with Abortus Imminens. In addition, this study also presents the first research conducted on ADA enzyme activity in Abortus Imminens patients. Therefore, this study represents an important contribution to the literature.

In conclusion, oxidative stress due to low GST and GR levels may play an important role in the pathogenesis of Abortus Imminens. In this study, the literature is the first work.

#### Declaration of Interests

The authors declare no conflict of interest.

#### Statement of Human and Animal Rights

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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